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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY-DOCKET NO.	CONFIRMATION NO.
10/008,571	12/03/2001	Ian Tomlinson	8039/1125	6655
<div>29933      7590      02/04/2008</div> <div>PALMER &amp; DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199</div> <div>EXAMINER STEELE, AMBER D</div> <div>ART UNIT      PAPER NUMBER</div> <div>1639</div> <div>MAIL DATE      DELIVERY MODE</div> <div>02/04/2008      PAPER</div>				

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/008,571

Applicant(s)

TOMLINSON ET AL.

Examiner

Amber D. Steele

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 11,17 and 54-64 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11,17 and 54-64 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☒ Certified copies of the priority documents have been received in Application No. 09/888,313.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of the Claims***

1. The amendment to the claims received on July 10, 2006 canceled claims 1-10, 12-16, and 18-53 and amended claims 11 and 17.

The amendment to the claims received on February 2, 2007 added new claims 54-64.

The amendment to the claims received on November 5, 2007 amended claims 11 and 17.

Claims 11, 17, and 54-64 are currently pending and under consideration.

### ***Priority***

2. The present application claims status as a CIP of U.S. application 09/888,313 filed June 22, 2001 and benefit of U.S. provisional application 60/246,851 filed November 8, 2000. The present application also claims foreign priority to UK 0015443.5 filed June 23, 2000 and UK 0026099.2 filed October 25, 2000.

### ***Invention as Claimed***

3. A method for creating a combinatorial library of two-chain polypeptides, wherein each two-chain polypeptide of said library comprises one member of a first repertoire of single chain polypeptides and one member of a second repertoire of single chain polypeptides, the method comprising the step of providing an array comprising a solid surface that includes said first repertoire of single chain polypeptides deposited on the solid surface in a first series of continuous lines that do not intersect with each other and said second repertoire of single chain polypeptides deposited on the solid surface in a second series of continuous lines that do not intersect with each other wherein each line of the first series of lines intersects with each line of the second series of lines such that each member of the first repertoire is juxtaposed with each

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member of the second repertoire such that members of the first repertoire are able to interact with members of the second repertoire thereby generating a two-chain polypeptides at the intersection of said first and second series of lines thereby creating a combinatorial library of two-chain polypeptides or alternatively depositing a third repertoire of single-chain polypeptides on the surface in a third series of continuous lines that do not intersect each other and juxtaposing the third repertoire such that the members of the first, second, and third repertoires are able to interact thereby generating three-chain polypeptides and variations thereof.

#### **Withdrawn Objection**

4. The objection to the disclosure regarding the citation for the de Wildt reference on page 55 is withdrawn in view of the amendment to the specification received on November 5, 2007.

#### **Withdrawn Rejections**

5. The rejection of claims 11, 17, and 54-64 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention regarding juxtaposed is withdrawn in view of the amendments to the claimed received on November 5, 2007 (i.e. juxtaposed with each member...such that members of one repertoire are able to interact with members of at least another repertoire).
6. The rejection of claims 17 and 64 under 35 U.S.C. 102(b) as being anticipated by Bussow et al. Nucleic Acids Research 26(21): 5007-5008, 1998 is withdrawn upon further consideration (i.e. a stream is not a third series of continuous lines). Please note: the rejection of claim 11 under 35 U.S.C. 102(b) as being anticipated by Bussow et al. Nucleic Acids Research 26(21): 5007-5008, 1998 is maintained (see below).

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7. The rejection of claims 11, 17, and 54-64 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 11-14, and 42 of copending Application No. 10/161,144 is withdrawn in view of the abandonment of the application on September 11, 2007.

#### **Maintained Rejections**

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Please note: the rejections may have been altered to reflect the claim amendments received on November 5, 2007.

#### ***Claim Rejections - 35 USC § 112***

9. Claims 11, 17, and 54-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "continuous lines" in claims 11 and 17 is a relative term which renders the claim indefinite. The term "continuous line" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The present specification defines a line as preferably "XX long and YY wide" which can be straight, curved, circles, polygons, radial lines, stream, channel, flow, tubes, tubing, droplets which coalesce, spray, or a tube with a lumen (please refer to page 4, last paragraph; page 5, page 26, first paragraph). The dimension of "XX" and "YY" would not be readily ascertained by one of skill in the art. For example, a "line" "XX long and YY wide" made of "a series of droplets" that "coalesce" into a "circle" could be a spot (i.e. wherein the width of the spots are such that the droplets coalesce into a continuous line

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forming a circle wherein the center of the circle is filled in); a line could be a centrifuge “tube” with a “lumen into which a member of a repertoire useful in the inventions is placed”; a line could be a streak on a plate, a line could be a lane in a gel, etc.

### *Arguments and Response*

10. Applicants’ arguments directed to the rejection under 35 USC 112, second paragraph (indefinite), for claims 11, 17, and 54-64 were considered but are not persuasive for the following reasons.

Applicants contend that the definition of line and continuous in the specification is definite. In addition, applicants contend that droplets coalescing to form a continuous line of solution which may be a circle can not be interpreted as a spot. Applicants also contend that XX and YY dimensions are definite because XX and YY are length and width, respectively as opposed to dimensions of diameter, radius, or perimeter (i.e. measurements of a spot).

Applicants’ arguments are not convincing since the definitions of continuous and lines in the present specification render the terms indefinite. Specifically, droplets that coalesce to form a continuous line which may be a circle could also coalesce into a spot dependent on the dimensions of the spot/line (i.e. XX long by YY wide; distance between one end of the line and the other end of the line is such that the middle of the circle fills in). Regarding the use of XX and YY to indicate line dimensions (i.e. length and width) and not that of a spot, it is noted that an irregular spot (i.e. oval) could be measured in length and width. In addition, a circular line could also be measured in terms of length and width. There is no reference in the specification that the length (i.e. XX) need be longer than the width (i.e. YY) as would be necessary in the

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standard definition of a line. Furthermore, a continuous line of the present definition could be a square or a rectangular shaped "spot" on a surface.

***Claim Rejections - 35 USC § 102***

11. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Bussow et al.

Nucleic Acids Research 26(21): 5007-5008, 1998.

For present claim 11, Bussow et al. teach a picking/gridding robot that gridded onto filter membranes cells expressing proteins (e.g. first or second repertoire of single-chain polypeptides, lines on grid from left to right and/or second repertoire of single-chain polypeptides, lines on grid from top to bottom; juxtaposed) and monoclonal antibodies thus creating two-chain polypeptides (please refer to entire disclosure particularly page 5007, third and fourth paragraphs; page 5008, third full paragraph).

Therefore, the presently claimed invention is anticipated by the teachings of Bussow et al.

***Arguments and Response***

12. Applicants' arguments directed to the rejection under 35 USC 102 (b) as being anticipated by Bussow et al. for claim 11 were considered but are not persuasive for the following reasons.

Applicants contend that Bussow et al. teach gridding bacterial colonies on a surface which applicants contend is spotting and not forming continuous lines.

Applicants' arguments are not convincing since the teachings of Bussow et al. anticipate the method of the instant claims. Bussow et al. teach gridding (please refer to the entire

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specification particularly the abstract; page 5007; Figure 1). A grid is defined as “a network of uniformly spaced horizontal and perpendicular lines” (see definition of grid from the Merriam-Webster Online Dictionary). Thus, gridding is a method of forming a first series of continuous lines that do not intersect each other and forming a second series of continuous lines that do not intersect each other such that the first and second lines are juxtaposed allowing the first and second lines to interact.

13. Claims 11, 17, 54-56, 59-61, and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Rowe et al. Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS).

For present claims 11, 17, 54-56, 59-61, and 64, Rowe et al. teach methods of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor wherein vertical channels comprise antibodies and adding samples flowed through horizontal channels (e.g. single-chain polypeptides; first repertoire, second repertoire, and/or third repertoire; continuous lines that may be at 179° angles if two single-chain polypeptides per channel to make VH-VL for example) wherein the vertical and horizontal channels are at 90° angles (please refer to entire reference particularly Figure 1; experimental section).

Therefore, the presently claimed invention is anticipated by the teachings of Rowe et al.

#### ***Arguments and Response***

14. Applicants' arguments directed to the rejection under 35 USC 102 (b) as being anticipated by Rowe et al. for claims 11, 17, 54-56, 59-61, and 64 were considered but are not persuasive for the following reasons.



Applicants contend that Rowe et al. teach patterning of capture antibodies in vertical stripes on a surface, but do not teach a second or third series of continuous lines. Applicants contend that the analyte flowed through horizontally oriented channels (i.e. stream of fluid is a continuous line; see definitions in the present specification) is not “deposited” (i.e. defined as placing a member of a repertoire of the present invention on a solid surface such that the member becomes stably associated with the surface via covalent bonds, hydrogen bonds, or ionic interactions; see page 31 of the present specification).

Applicants’ arguments are not convincing since the teachings of Rowe et al. anticipate the method of the instant claims. Rowe et al. teach continuous lines (i.e. vertical stripes) of captured (i.e. deposited) antibodies-biotin-avidin on a solid surface, continuous lines (i.e. horizontal stripes) of analyte (i.e. BSA blocker and sample; continuous line of reagents wherein BSA is bound in sections between the vertical stripes and/or non-antigen binding portions of the antibody and samples bound to antibodies on the vertical stripes where the horizontal stripes intersect the vertical stripes; continuous line as the stream is flowing; based on the strength of the bonds and the wash conditions, the bonds may be stable), and continuous lines of detector antibody (please refer to the entire specification particularly Experimental Section; Figure 1). Furthermore, in the interview on September 5, 2007, applicants’ representative stated that the continuous lines could have varying concentrations of polypeptide wherein the lower limit of the concentration is zero (i.e. absence of polypeptide along the “continuous” line).

The Office does not have the facilities (i.e. lab) to provide the factual evidence needed in order to determine if the stream is “deposited” (i.e. forms covalent bonds, hydrogen bonds, or ionic interactions). In the absence of evidence to the contrary and because the apparatus for

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performing the screening method taught by Rowe et al. otherwise meet the claimed structural limitations, the burden is upon the applicant to prove that the stream at no point in time “deposits” under any wash conditions the reagents utilized in the method taught by Rowe et al. and to establish the patentable differences. See *In re Best* 562F.2d 1252, 195 U. S. P. Q. 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922(PTO Bd.Pat. App. & Int. 1989.

***Claim Rejections - 35 USC § 103***

15. Claims 11, 17, and 54-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rowe et al. Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS) and Stevens et al. U.S. Patent 6,485,943 filed March 22, 1999.

For present claims 11, 17, 54-56, 59-61, and 64, Rowe et al. teach methods of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor wherein vertical channels comprise antibodies and adding samples flowed through horizontal channels (e.g. single-chain polypeptides; first repertoire and/or second repertoire; continuous lines that may be at 179° angles if two single-chain polypeptides per channel to make VH-VL for example) wherein the vertical and horizontal channels are at 90° angles (please refer to entire reference particularly Figure 1; experimental section).

However, Rowe et al. does not specifically teach making VH-VH or VL-VL two-chain polypeptides or the VH-VH or VL-VL two-chain polypeptides bound to antigen to make three-chain polypeptides.

For present claims 57-58 and 62-63, Stevens et al. teach methods of making recombinant antibody subunit dimers including VH-VH and VL-VL and screening against antigen comprising

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providing VH and/or VL and interacting the VH and/or VL (please refer to entire specification particularly abstract; column 4, lines 44-67; column 5, lines 1-9; column 6, lines 20-41; column 7, lines 23-36; columns 9-10).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al.

One having ordinary skill in the art would have been motivated to do this because Rowe et al. teach that immunosensors are easy to use, provide rapid assay times, have sensitivity comparable to ELISA, and can be utilized to study multianalyte binding (please refer to introduction and conclusion sections). In addition, Stevens et al. teach homologous dimerization of antibody subunits and altering amino acid sequences in the interfacial segments to improve yields of Fab and Fv products and studying the interactions via dimerization assays/screens (please refer to columns 4-5).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. because Rowe et al. teach utilizing immunosensors to study multianalyte interactions (e.g. VH, VL, antigen, dimmers, trimers; please refer to conclusion).

Therefore, the modification of the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. render the instant claims *prima facie* obvious.

*Arguments and Response*

16. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Rowe et al. Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS) and Stevens et al. U.S. Patent 6,485,943 filed March 22, 1999 for claims 11, 17, and 54-6 were considered but are not persuasive for the following reasons.

Applicants contend that Rowe et al. teach patterning of capture antibodies in vertical stripes on a surface, but do not teach a second or third series of continuous lines and that Stevens et al. does not teach these alleged deficiencies.

Applicants' arguments are not convincing since the teachings of Rowe et al. and Stevens et al. render the method of the instant claims *prima facie* obvious. Applicants' arguments are not convincing since the teachings of Rowe et al. anticipate the method of the instant claims. Rowe et al. teach continuous lines (i.e. vertical stripes) of captured (i.e. deposited) antibodies-biotin-avidin on a solid surface, continuous lines (i.e. horizontal stripes) of analyte (i.e. BSA blocker and sample; continuous line of reagents wherein BSA is bound in sections between the vertical stripes and/or non-antigen binding portions of the antibody and samples bound to antibodies on the vertical stripes where the horizontal stripes intersect the vertical stripes; continuous line as the stream is flowing; based on the strength of the bonds and the wash conditions, the bonds may be stable), and continuous lines of detector antibody (please refer to the entire specification particularly Experimental Section; Figure 1). Furthermore, in the interview on September 5, 2007, applicants' representative stated that the continuous lines could have varying concentrations of polypeptide wherein the lower limit of the concentration is zero (i.e. absence of polypeptide along the "continuous" line). In addition, Stevens et al. teach making VH-VH or

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VL-VL two-chain polypeptides or the VH-VH or VL-VL two-chain polypeptides bound to antigen to make three-chain polypeptides.

The Office does not have the facilities (i.e. lab) to provide the factual evidence needed in order to determine if the stream is “deposited” (i.e. forms covalent bonds, hydrogen bonds, or ionic interactions). In the absence of evidence to the contrary and because the apparatus for performing the screening method taught by Rowe et al. otherwise meet the claimed structural limitations, the burden is upon the applicant to prove that the stream at no point in time “deposits” under any wash conditions the reagents utilized in the method taught by Rowe et al. and to establish the patentable differences. See *In re Best* 562 F.2d 1252, 195 U. S. P. Q. 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922 (PTO Bd. Pat. App. & Int. 1989).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

### **New Rejections Necessitated by Amendment**

#### ***Claim Rejections - 35 USC § 103***

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

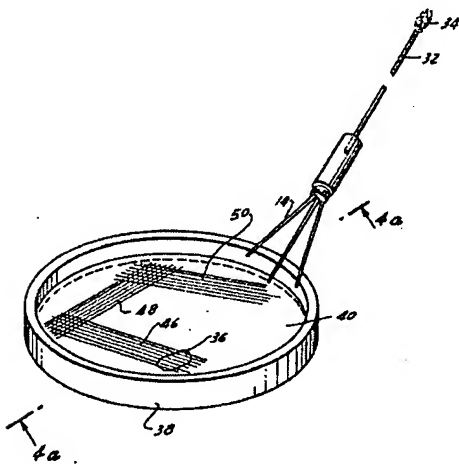
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18. Claims 11, 17, 54-56, 59-61, and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skerra et al. Analytical Biochemistry 196: 151-155, 1991 and Pardos U.S. Patent 4,010,077 issued March 1, 1977.

For present claims 11, 17, 54-56, 59-61, and 64 Skerra et al. teach a filter screening method comprising streaking a petri dish containing agar and a membrane with bacterial colonies expressing Fab fragments (i.e. VH and VL) wherein streaking is done with a metal loop, adding antigen to a membrane, and adding another membrane with other antibodies (i.e. sandwich ELISA, triple sandwich ELISA; please refer to the entire specification particularly the Materials and Methods section and Figures 1-3).

However, Skerra et al. does not specifically teach streaking multiple continuous lines.

For present claims 11 and 17, Pardos teach an inoculating loop with multiple fingers which streaks multiple continuous lines of the same or different samples (please refer to the entire specification particularly Figures 2-4; column 2, lines 3-45; column 3, lines 63-67; column 4, lines 1-11; see below).



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The claim would have been obvious because the substitution of one known element (i.e. metal loop) for another (i.e. inoculation loop with multiple fingers) would have yielded predictable results to one of ordinary skill in the art at the time of the invention. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

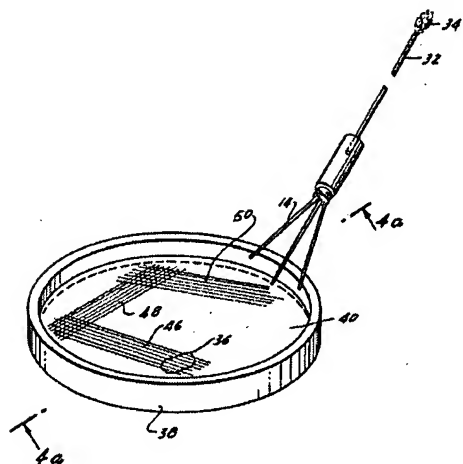
19. Claims 11, 17, 54-56, 59-61, and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rodenburg et al. Hybridoma 17(1): 1-8, 1998 and Pardos U.S. Patent 4,010,077 issued March 1, 1977.

For present claims 11, 17, 54-56, 59-61, and 64 Rodenburg et al. teach modified colony-lift methods comprising plating bacterial cells transformed with scFv/phagemid constructs onto agar plates, transferring the colonies to a membrane (i.e. nitrocellulose), coating a membrane with antigen, and adding another antibody to the membrane (please refer to the entire specification particularly the Materials and Methods section; Figure 1).

However, Rodenburg et al. does not specifically teach the manner of plating (i.e. continuous lines).

For present claims 11 and 17, Pardos teach an inoculating loop with multiple fingers which streaks multiple continuous lines of the same or different samples (please refer to the entire specification particularly Figures 2-4; column 2, lines 3-45; column 3, lines 63-67; column 4, lines 1-11; see below).

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The claim would have been obvious because the substitution of one known element (i.e. plating bacterial cells with an inoculation loop or via pouring liquid on an agar plate) for another (i.e. inoculation loop with multiple fingers) would have yielded predictable results to one of ordinary skill in the art at the time of the invention. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

### **Maintained Rejections**

20. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Please note: the rejections may have been altered to reflect the claim amendments received on November 5, 2007.

### ***Double Patenting***

21. Claims 11, 17, and 54-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 10/161,145. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the present invention and the invention of U.S. application 10/161,145 are drawn to methods comprising arraying a plurality of polypeptides on



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a support which can be single-chain or two-chain, arraying a second plurality of polypeptides/targets on a support which can be single-chain, and juxtaposing the supports so that either two-chain or three-chain polypeptides are produced (please note: three-chain polypeptides read on antibodies bound to antigens as defined in the present specification; two-chain polypeptides read on scFv bound to antigen).

For present claims 11, 17, and 54-64, U.S. application 10/161,145 claim immobilizing target molecules on a first support wherein the target molecules can be protein, polypeptide, amino acid, whole cell or cell extract (e.g. antigen, single-chain polypeptide, VH, VL), arraying a plurality of polypeptides on a second support wherein the polypeptides can be antibodies (e.g. VH, VL, VH-VL, VH-VH, VL-VL), juxtaposing the first and second supports wherein binding can occur (e.g. making a two-chain or three-chain polypeptide library; please refer to claims 1-18).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Arguments and Response***

22. Applicants' arguments directed to the rejection on the ground as of nonstatutory obviousness-type double patenting (i.e. provisional) for claims 11, 17, and 54-64 were considered but are not persuasive for the following reasons.

Applicants contend that U.S. application 10/161,145 claim arraying nucleic acids and thus could not make two- or three-chain polypeptides.

Applicants' arguments are not convincing since the claims of U.S. application 10/161,145 render the method of the instant claims *prima facie* obvious. While U.S. application 10/161,145

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does claim arraying a plurality of nucleic acid molecules (i.e. claim 1, method step b; claim 18), the arrayed nucleic acid molecules are expressed to produce polypeptides such that the polypeptides come into contact with target molecules (i.e. claim 1, method step d; claim 18, method step d; see also claims 2-5 and 8-9) wherein the target molecules can be protein, polypeptide, enzyme, amino acid, etc. (see claim 15).

23. Claims 11, 17, and 54-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 11/413,427. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. application 11/413,427 are drawn to methods comprising arranging a first repertoire in at least one first series of continuous lines, arranging a second repertoire in at least one second series of continuous lines forming an array wherein the first and second lines intersect thereby juxtaposing the first and second repertoires (please note: three-chain polypeptides read on antibodies bound to antigens as defined in the present specification; two-chain polypeptides read on scFv bound to antigen).

For present claims 11, 17, and 54-64, U.S. application 11/413,427 claims a method comprising arranging a first repertoire in at least one first series of continuous lines wherein the first repertoire can be VH or VL, arranging a second repertoire in at least one second series of continuous lines wherein the second repertoire can be VH or VL, forming an array wherein the first and second lines intersect thereby juxtaposing the first and second repertoires, optionally

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contacting the array with target (e.g. antigen), and allowing binding to create two- or three-chain polypeptides (please refer to claims 1-23).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Arguments and Response*

24. Applicants' arguments directed to the rejection on the ground as of nonstatutory obviousness-type double patenting (i.e. provisional) for claims 11, 17, and 54-64 were considered but are not persuasive for the following reasons.

Applicants contend that upon notification of allowable subject matter, the applicants will consider filing a terminal disclaimer.

Applicants' arguments are not convincing since the claims of U.S. application 11/413,427 render the method of the instant claims *prima facie* obvious and the rejection will not be held in abeyance.

25. Claims 11, 17, and 54-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56-68 and 78-86 of copending Application No. 09/888,313. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. application 09/888,313 are drawn to methods comprising arranging a first repertoire in a series of continuous lines, arranging a second repertoire in a series of continuous lines, and forming an array via intersecting the lines and juxtaposing the first and

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second repertoires (please note: three-chain polypeptides read on antibodies bound to antigens as defined in the present specification; two-chain polypeptides read on scFv bound to antigen).

For present claims 11, 17, and 54-64, U.S. application 09/888,313 claims a method comprising arranging a first repertoire in a series of continuous lines wherein the first repertoire can be VH or VL, arranging a second repertoire in a series of continuous lines wherein the second repertoire can be VH or VL, optionally, forming an array via intersecting the lines and juxtaposing the first and second repertoires, and optionally contacting the array with a target epitope (e.g. antigen, forming two- or three-chain polypeptides; please refer to claims 56-68 and 78-86)

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

#### ***Arguments and Response***

26. Applicants' arguments directed to the rejection on the ground as of nonstatutory obviousness-type double patenting (i.e. provisional) for claims 11, 17, and 54-64 were considered but are not persuasive for the following reasons.

Applicants contend that upon notification of allowable subject matter, the applicants will consider filing a terminal disclaimer.

Applicants' arguments are not convincing since the claims of U.S. application 09/888,313 render the method of the instant claims *prima facie* obvious and the rejection will not be held in abeyance.

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***Conclusion***

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS

January 23, 2008

/Jon D. Epperson/

Primary Examiner, AU 1639